Approved 8/29/02

U.S. Environmental Protection Agency
Science Advisory Board
Environmental Health Committee (EHC)
Trichloroethylene Health Risk Assessment: Synthesis and Characterization Review Panel

Summary Minutes of Public Teleconference
Date: July 18, 2002

Committee Members: (See Roster - Attachment A.)
Date and Time: 1 pm to 3 pm, July 18, 2002 (See Federal Register Notice - Attachment B).
Location: Ariel Rios North, Conference Room 6013
Purpose: The purpose of this public teleconference meeting was to:(a) discuss substantive issues related to a draft Panel report date July 15, 2002 and (b) to identify a process for reaching closure on editorial changes to the document to be sent to the Executive Committee for review.
Attendees: Chair: Dr. Henry Anderson;

Panel Members: (EHC Members) Dr. Dale Hattis, Dr. George Lambert,, Dr. Abby Li; and Dr. Ulrike Luderer; (SAB Consultants) Dr. Susan J. Borghoff, Dr. Lutz Edler, Dr. Michael McClain; Dr. Gina Solomon and Dr. Gina Solomon; (Federal Experts)y Dr. Ronald Melnick.

EPA SAB Staff: Dr. Angela Nugent, (DFO for the Panel), (Management Assistant for the Panel), Dr. Vanessa Vu

Other Persons on the Agenda: Dr. V. James Cogliano (EPA, Office of Research and Development) and Dr. Paul Dugard (Halogenated Solvents Industry Alliance, Inc);

Other persons as noted on the sign-in sheet and TCE Teleconference attendance sheet.

Meeting Summary:

The discussion generally followed the issues and general timing as presented in the meeting Agenda (see Meeting Agenda - Attachment C). The teleconference lasted until 2:55 pm. There was one set of written public comments submitted to the Committee (Attachment D: Comments from George Alapas to Vanessa Vu, July 17, 2002), and there was one request to present public comments during the discussion.

Welcome and Roll Call. Dr. Henry Anderson, the Chair, opened the session at 1:05 p.m. welcoming panel members (Roster, Attachment A), and reviewed the agenda (Attachment C). Dr. Angela Nugent, Designated Federal Official (DFO) took roll.

Introductory Remarks. Dr. Anderson identified the major goal of the meeting as providing an opportunity for panel members to identify substantive issues and issues that have been omitted. He then described the plan for completing the report. He asked panel members to identify changes to the DFO by August 5, 2002; the DFO and the Chair would synthesize

comments and send a "final draft" out by August 12, 2002 (this draft would flag the substantive changes made); and then Panel Members would have an opportunity to identify their last issues by August 23, 2002. The Draft would then go the SAB Executive Committee for their review before sending the report to the Administrator.

He then asked the Panel to focus on the substantive issues identified in the agenda and then to raise other issues for discussion

Uncertainty factors for RfD and RfCs. The Panel generally supported the reorganization in the draft document that placed detailed information about the uncertainty factors in a new Appendix and noted the usefulness of Table 1. A few panel members, however, suggested that the main text needed to highlight the uniqueness of EPA's construction of the uncertainty factors, based on consideration of multiple endpoints. Dr. Li and Dr. Luderer volunteered to work together to provide text appropriate to Section 6.2.3 on this point.

Panel members then discussed the need to identify more clearly the most significant points of difference among panel members regarding the issue of adding a children's safety factor. Dr. Li volunteered to provide text to add to the discussion on page 37. Dr. Vu asked the Panel if it was aware that the uncertainty factor for human variation was intended to cover all life stages and that the children's factor was intended to be used if the database was not good enough to say "yea or nay." Panel members responded that they were aware of these considerations and that their discussion explicitly addressed them.

Panel members suggested that section 6.2.3. could benefit from use of subheadings drawn from Table 1. One Panel member noted that Table 1 should show that additional information on the human variation uncertainty factor should appear in Appendix B. The Panel asked that appendices A and B be reversed in sequence.

Uncertainty factor for children. The Panel discussed first whether it had a consensus on the following question: "Are there issues with children that put them at a greater risk than adults?" The Panel acknowledged that there was ambiguous data, but that the toxicology data and data from other chemicals suggested that they could be at greater risk.

The Panel then focused on the second part of charge question 9:"How can this be reflected in the quantitative assessment?" Another member reframed this question as "Given the uncertainty in the data, do the animal data together with uncertainties in other data, indicate the possibility for greater susceptibility?" One member emphasized the importance of polling the panel in regard to this question. Several Panel members answered yes. One panel member stated that she was not convinced there should be an additional uncertainty factor, based on current evidence. In her view, differential exposures should not be factored in; sometimes the data for chemicals show that enzymatic differences for children can work for or against a chemical; that where the mode of action is peroxisome proliferation, she has a "hard time thinking kids are more susceptible," and that generally more data are needed before a determination can be made.

Another member agreed that the Panel is having difficulty agreeing on "going quantitative" without more of a quantitative context. He noted his view that there was some evidence of pharmacokinetic variability in the direction of very young neonates being very sensitive. He stated that if TCE is the active metabolite for birth rate reduction, then that is of some special concern that could justify a special factor. Dr. Hattis committed to providing a paragraph on this point. He also suggested that the Panel can "point to the direction for deriving" a factor for children, but that it cannot derive it in its Panel report.

Another member thought the structure of the current draft was strong and could be enhanced by a step-by-step discussion of the topics of exposure, absorption, and end organ toxicity. For each, there should be more explicit discussion of areas where children are at greater toxicity, existing data and data gaps, and a discussion of the range of views expressed by panel members regarding how the evidence may affect the uncertainty factor for children.

A different view was expressed by another member, who suggested that the RfD discussion be removed entirely from Section 11 of the Report. The Panel discussed the pros and cons of both approaches. The sense of the group was to retain references in both sections 6 and 11 and to include the extended discussion in Section 11. The extended discussion would incorporate the step-by-step discussion mentioned in the paragraph above. Dr. Lambert agreed to provide this text.

Dr. Michael Firestone from the Office of Children's Health Protection asked if the panel in its report could differentiate between data deficiencies for TCE vs. general data deficiencies related to children's risk. Panel members responded that they had not discussed this issue and that it would be appropriate as a topic for another Panel.

Text discussion of cancer classification, Section 4.2. Although one member thought section 4.2. did a nice job of capturing the Panel's range of views, several others expressed discomfort with section 4.2. One member stated that lines 25 and 26 were not clear and disagreed with sentences on line 17 and 18, given issues pointed out relative to the epidemiology data, and that uncertainties with the Henschler data need to be cleared up Another member seconded that view, saying that the section raised a red flag, and noted that she understood that the Panel had made an explicit decision at the June meeting not to discuss the cancer classification.

Another member explained the logic she saw behind section 4.2. It was meant to be a "big picture" summary of the issues discussed later in the chapter. It was intended to give the bottom line of what the Panel thought of the Agency's qualitative assessment. She agreed that there wasn't a focus ed discussion of the cancer classification, but points related to it were "speckled through the discussion."

One member stated that her view was that the Agency's characterization wasn't solid enough because it was not supported by adequate quantitative data. She thought a more appropriate characterization was "likely at high doses, unlikely at low doses."

The Panel then briefly discussed different elements of the weight of evidence: that the toxicity for the human liver was strong; that the epidemiological data for the liver was not strong--a relationship existed at relatively low doses and no causal relationship was determined; and that the one tumor found in the toxicity tests that was relevant to humans was the kidney but there was no strong association in the epidemiology literature for the kidney. There was concern about reflecting views about likely hood of response at different doses.

Some panel members expressed frustration that they had not discussed the classification at the meeting and that the draft report includes text on this issue. Dr. Vu pointed out to the Panel that the minutes from the Panel's meeting June 18-19 documented the Panel's discussions regarding the cancer classification. She pointed out that she and Dr. James Cogliano had informed the Panel that the cancer guidelines were in flux and that the Agency had intended to use whatever categories and criteria existed at the time the TCE assessment was finalized in establishing the classification for TCE

The Panel agreed to revise the text currently in section 4.2. The Chair and the DFO would move the sentence "Several panel members characterized..." currently on line 34, page 22

to a spot later on in the chapter, or to the section in section 7.2.3, Linear or Nonlinear Approach. Dr. Luderer agreed to work with Dr. Hattis on the language to be included in the range of views discussion that might be placed in section 7.2.3. The paragraph would include a more complete description of the range of views expressed by panel members, including the views about toxicity at high and low doses.. Panel Members will send the DFO suggestions for specific language to be included in that discussion of range of views. The paragraph would also clarify that Agency did not ask the panel to address the classification issue in a charge question, and that the Panel did not devote significant time to the issue on the agenda.

Agency Response to the July 15, 2002 Draft. Dr. James Cogliano thanked the Panel on behalf of the Agency for its thoughtful and thorough advice. He assured the Panel that the Agency will address their comments, the comments of the state-of-the-science authors and public comments before the document is finalized. He also pointed out that the Agency will benefit from the report as it develops the cancer guidelines, approaches to children's risk assessment, and cumulative risk approaches.

Public Comment. Dr. Paul Dugard acknowledged the substantial document produced quickly by the Panel. He asked if the Panel had considered asking the Agency to review the revised document when complete. He suggested that EPA's use of complex epidemiology and pharmacokinetic data could benefit from consultation with others. He indicated that the Halogenated Solvents Industry Alliance would be interested in facilitating such an interaction.

The Panel chair then noted that the Panel was completing its work with this review report. If the Agency wishes additional review, that would bes its prerogative. The Panel is advising the Agency to move forward with the risk assessment.

Other Substantive Issues. One member noted that the cover letter might advise the Agency to move quickly, and that perhaps it could add a phrase such as "as expeditiously as possible" to the second paragraph on page 3. No objections were noted.

Discussion of Process for Completing Work on the Document. The Chair asked members to cc the DFO on email exchanges among the panel exploring language changes. He asked that any changes panel members wish to see in the final document be sent to the DFO by August 5 marked as final changes.

Action items:

1. Dr. Li and Dr. Luderer to work together to provide text for Section 6.2.3 to highlight the uniqueness of EPA's construction of the uncertainty factors, based on consideration of multiple endpoints.
2. Dr. Li to provide text to add to the discussion on page 37 to identify more clearly points of difference among panel members regarding the issue of adding a children's safety factor.
3. Dr. Hattis to provide text for Chapter 11 to document his view that there was some evidence of pharmacokinetic variability in the direction of very young neonates being very sensitive and that, if TCE s the active metabolite for birth rate reduction, then that is

of some special concern that could justify a special factor.

4. Dr. Lambert to provide text for Chapter 11 that would provide a step-by-step discussion of the topics of exposure, absorption, and end organ toxicity. For each, there should be more explicit discussion of areas where children are at greater toxicity, existing data and data gaps, and a discussion of the range of views expressed by panel members regarding how the evidence may affect the issue of an uncertainty factor for children..
5. The Chair and the DFO would move the sentence "Several panel members characterized..." currently on line 34, page 22 to a spot later on in the chapter, or to the section in section 7.2.3, Linear or Nonlinear Approach. The paragraph would include a more complete description of the range of views expressed by panel members, including the views about toxicity at high and low doses..
6. Panel Members will send the DFO suggestions for specific language to be included in that discussion of range of views related to the cancer classification
7. Dr. Luderer and Dr. Hattis will provide language to discuss the range of views on cancer classification that would be appropriate to include in section 7.2.3, Linear or Nonlinear Approach.
8. Panel members to send information on missing references and editorial changes to the DFO by August 5.

At 2:35 p.m., Dr. Anderson adjourned the meeting.

Respectfully Submitted:

/ Signed /

Dr. Angela Nugent
Designated Federal Official

Certified as True:

/ Signed /

Dr. Henry Anderson, Chair

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by the Panel members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect definitive consensus advice from the Panel Members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters, or reports prepared and transmitted to the EPA Administrator following the public meetings.